

**Summary Minutes of the
Pulmonary-Allergy Drugs Advisory Committee
June 23, 2011**

Location: Washington DC/Silver Spring Hilton, The Ballrooms, Silver Spring, MD

All external requests for the meeting transcripts should be submitted to the CDER, Freedom of Information office.

These summary minutes for the June 23, 2011 meeting of the Pulmonary-Allergy Drugs Advisory Committee of the Food and Drug Administration were approved on July 25, 2011.

I certify that I attended the June 23, 2011 meeting of the Pulmonary-Allergy Drugs Advisory Committee of the Food and Drug Administration and that these minutes accurately reflect what transpired.

**_____/s/_____
Kristine Khuc, Pharm.D.
Designated Federal Officer, PADAC**

**_____/s/_____
Jerry Krishnan, M.D., Ph.D.
Committee Chair, PADAC**

FOOD AND DRUG ADMINISTRATION (FDA)
Center for Drug Evaluation and Research (CDER)
Pulmonary-Allergy Drugs Advisory Committee (PADAC)
Hilton Washington DC/Silver Spring, The Ballrooms
Silver Spring, Maryland
June 23, 2011
Summary Minutes

The Pulmonary-Allergy Drugs Advisory Committee (PADAC) met on June 23, 2011 at the Hilton Washington DC/Silver Spring, The Ballrooms, Silver Spring, Maryland. Prior to the meeting, the members and the invited consultants had been provided the background materials from the FDA and Sponsor. The meeting was called to order by Jerry Krishnan, M.D., Ph.D., (Chair); the conflict of interest statement was read into the record by Kristine Khuc, Pharm.D. (Designated Federal Officer). There were approximately 125 persons in attendance. There were eight speakers for the Open Public Hearing session.

Attendance:

Pulmonary-Allergy Drugs Advisory Committee Members Present (Voting):

Paul Greenberger, M.D., David Jacoby, M.D., Jerry Krishnan, M.D., Ph.D. (Chair), David Mauger, Ph.D., Rodney Mullins (Consumer Representative), Thomas Alexander Platts-Mills, M.D., Ph.D., Kelly Stone, M.D., Ph.D.

Temporary Non-Voting Member Present:

Ellen Strahlman, M.D. (Acting Industry Representative)

Special Government Employee Consultants Present (Temporary Voting Members):

Larry Borish, M.D., Michael Foggs, M.D., Jay Portnoy, M.D., Philip Posner, Ph.D. (Patient Representative), Gillian Shepherd, M.D., James Tracy, D.O.

FDA Participants Present (Non-Voting):

Joan Buencosejo, Ph.D., Badrul Chowdhury, M.D., Ph.D., Susan Limb, M.D., Brian Porter, M.D., Ph.D., M.P.H., Curtis Rosebraugh, M.D.

Designated Federal Officer:

Kristine Khuc, Pharm.D.

Open Public Hearing Speakers:

Jenny Barnes, Amanda Dillon, Diane Dorman- National Organization for Rare Disorders (NORD)

Jacob Heis, H. Henry Li, M.D., Ph.D.- Institute for Asthma and Allergy

Janet Long- U.S. Hereditary Angioedema Association

Marcus Maurer, M.D.- Charite-Universitatsmedizin Berlin, Michelle Williamson

Issue: The committee discussed the new drug application (NDA) 22150, icatibant solution for injection (proposed tradename Firazyr), Shire Human Genetic Therapies, for the proposed indication of treatment of acute attacks of hereditary angioedema (HAE).

The agenda was as follows:

Call to Order
Introduction of Committee

Jerry Krishnan, M.D., Ph.D.
Chair, PADAC

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Conflict of Interest Statement	Kristine Khuc, Pharm.D. Designated Federal Officer, PADAC
Opening Remarks	Badrul Chowdhury, M.D., Ph.D. Director, Division of Pulmonary, Allergy, and Rheumatology Products, Center for Drug Evaluation and Research (CDER), FDA Susan Limb, M.D. Clinical Team Leader Division of Pulmonary, Allergy, and Rheumatology Products CDER, FDA
Sponsor Presentation	Shire Human Genetic Therapies
Introduction	Philip Vickers, Ph.D. Sr. Vice President of Research & Development Shire HGT
HAE Unmet Medical Needs	William Lumry, M.D. Clinical Professor, Internal Medicine/Allergy Division University of Texas Southwestern Medical School Dallas, Texas
Efficacy and Safety of Icatibant	Sue Cammarata, M.D. Vice President, Clinical Affairs Shire HGT
Icatibant Clinical Data-Relevance	Marc Riedl, M.D. Assistant Professor of Medicine Section Head, Clinical Immunology and Allergy UCLA-David Geffen School of Medicine
Conclusions	Sue Cammarata, M.D.
Questions for Clarification for Sponsor	
Break	

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FDA Presentation

Clinical Perspective- Efficacy	Brian Porter, M.D., Ph.D., M.P.H Medical Officer, Division of Pulmonary, Allergy, and Rheumatology Products CDER, FDA
Statistical Perspective	Joan Buencosejo, Ph.D. Acting Statistical Team Leader, Division of Biometrics 2 CDER, FDA
Clinical Perspective- Safety	Brian Porter, M.D., Ph.D., M.P.H.
Questions for Clarification for FDA	
Lunch	
Open Public Hearing	
Charge to the Committee	Susan Limb, M.D.
Discussion and Questions to the Committee	
Break	
Continue Discussion and Questions to the Committee	
Adjourn	

Questions to the Committee:

1. Discuss the efficacy and safety data for icanitabant (**Discussion Question**)

A majority of the committee members commented on the following:

- *Lack of diversity among study subjects;*
- *Modest number of patient enrollment;*
- *Homogenous population studied and applicability of data in a real world setting;*
- *Maintain patient registry for safety data or to collect utilization data by various practitioners;*
- *Unblinding and comparison results from FAST 1 versus FAST 3. FAST 1 showed little evidence of a treatment effect due to either a placebo effect or incorrect patient population selected which may question the interpretation of results of FAST 3;*

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- *Parameter to judge efficacy is relevant when looking at patient onset of relief within 8 hours versus a longer duration;*
- *Using a single symptom relief score may be less bias.*

(Please see official transcript for details)

2. Do the data provide substantial and convincing evidence of a clinically meaningful benefit for icatibant in the treatment of acute attacks of hereditary angioedema? **(Voting Question)**

a. *If not, what further data should be obtained?*

YES: 12

NO: 1

ABSTAIN: 0

An overwhelming majority of the committee members voted “Yes” and remarked that the data was convincing and robust to demonstrate evidence of a clinically meaningful benefit of icatibant in treating acute attacks of HAE. The member who voted “No” felt that there was only a modest number of enrollments and that subgroups were not appropriately represented.

(Please see official transcript for details)

3. Has the safety of icatibant been adequately assessed for the treatment of acute attacks of hereditary angioedema? **(Voting Question)**

a. *If not, what further data should be obtained?*

YES: 11

NO: 1

ABSTAIN: 1

The majority of the committee members who voted “Yes” agreed that the safety of icatibant has been adequately evaluated. In addition, they also recommended maintaining a patient registry. One committee member abstained from voting and commented that safety was only demonstrated in a limited number of patients and would like to see further data in ischemic diseases, pregnant, and minority patients. Another committee member voted “No” and felt uncomfortable about the safety data and had concerns regarding the adverse event relating to the recurrence of HAE and the lack of data on other co-morbidities that may be relevant to this patient population.

(Please see official transcript for details)

4. Do the efficacy and safety data provide substantial evidence to support approval of icatibant for the treatment of acute attacks of hereditary angioedema in patients 18 years of age and older? **(Voting Question)**

a. *If not, what further data should be obtained?*

YES: 12

NO: 1

ABSTAIN: 0

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The overall majority of the committee members voted “Yes” and felt that there was substantial and convincing efficacy and safety evidence to support approval. Additionally, they also provided comments on the need for further teratology and reproductive investigations and advocated for a patient registry. One committee member voted “No” and stressed the need to further investigate cases on toxicity and dropout; and examine cases in pregnant patients.

(Please see official transcript for details)

5. Discuss the potential impact of self-administration on the safety and efficacy of icatibant, if any. **(Discussion Question)**

The committee members agreed that most hospital emergency rooms do not have the appropriate training and/or drugs to treat HAE patients when they seek care. The overall consensus of the committee is that patients are able to self-diagnose and perform self-drug administration in this specific disease state. They greatly emphasized the need to have intense patient education including proper administration techniques and had concerns relating to the dangers of health care professionals delaying medical treatment with icatibant. The committee also stressed that additional self-administration data would be very useful.

(Please see official transcript for details)

6.* Do the data support the self-administration of icatibant? **(Voting Question)**
a. *If not, what further data should be obtained?*

YES: 11

NO: 1

ABSTAIN: 1

*Question 6 was created due to a favorable consensus by the committee to provide their opinion on self-administration of icatibant through an official vote.

In general, the committee members voted “Yes” and strongly felt that there is support for self-administration of icatibant with the data available. One abstention came from a committee member on a technical ground that the member is not a treating physician. The other member who voted “No” commented on the need to further evaluate the appropriateness of self-administration in severe HAE patients.

(Please see official transcript for details)

Meeting adjourned at approximately 3:50 p.m.